REMARKS

Claims 1-41 are pending. Claims 1-31, 39 and 41 have been withdrawn from consideration. Claims 1, 2, 9, 10, 12, 13-18, 22-26, 28, 32-38 and 40 have been amended. Claims 42-44 have been added, based on original claims 7/8, and the disclosure at page 6, line 26, and page 11, lines 15-17. Claim 43 is readable on the elected species. Claims 1-44 remain in the case.

The specification has been checked, and all typographical errors have been corrected. Correction of the drawings and the submission of formal drawings will be delayed until allowable subject matter is indicated.

The examiner notes that applicants' election of Group II was without traverse. However, applicants did note that the Group I method of making claims would have to be rejoined and examined in this application, once the product claims of Group II are found allowable (*In re Ochiai*). Claims to Group A and Group B species that currently are withdrawn also will need to be examined, provided that the elected species of peptide platforms (from Group A) and anti-bacterial compounds (from Group B) are found allowable.

Claims 32-38 and 40 are rejected under the second paragraph of Section 112, the examiner alleging in this regard that it is not clear what is intended by the phrase "randomly-generated library." The terms "random" and "combinatorial" are both used to describe the libraries of glycopeptides generated under this invention. According to the invention, a peptide "scaffold" or "platform" with one or more sites for glycosylation is pre-synthesized and reacted with either a glycosyl donor or a mix of glycosyl donors in a single pot to facilitate combinatorial and random reactions. This method results in a random glycosylation at available sites and combinatorial formation of glycopeptides. The libraries consist of a large number of glycopeptides that arise from statistically possible combinations. The number of theoretically possible combinations may be calculated by the expression $(x + 1)^n$, where '**x**' is the number of glycosyl donors used in the one pot synthesis and '**n**' is the number of glycosylation sites on a peptide scaffold. The reactions between certain combinations may dominate the combinatorial synthesis. As a

consequence, the libraries consist of certain dominant products and some minor components. The components formed in these libraries are numerically of very large diversity and random. In order to more particularly point out and distinctly claim the present invention, applicants' have amended the claims to recite "a combinatorially-generated library of glycopeptides prepared by randomly reacting a peptide scaffold with either (1) carbohydrate structures associated with human cancer-associated mucins or (2) carbohydrate structures which function as adhesion ligands for bacterial receptors that are expressed on human cell surface antigens." In addition, claim 38 has been amended to eliminate the term "drug-like" and the claims have been amended to substitute the term "scaffold" for the term "platform." The recitation of "carcinoma-associated mucins" has been retained, as this term is defined in the specification and its scope is understood by those of skill in the art. The basis for the Section 112 rejection is believed to be obviated by the foregoing amendments and remarks, although if the examiner prefers, the phrase "carbohydrate structures associated with malignant cell antigens" could be substituted for "carcinoma-associated mucins," based on page 7, lines 28 and 29, of the disclosure.

Claims 32, 38 and 40 are rejected under Section 102(e), and claims 34-37 are rejected under Section 103(a), in each case based on Rao *et al.* (U.S. 5,795,958). Rao refers to "a collection or a library of peptide sequences to which a carbohydrate is covalently attached" (Rao at column 3, lines 15-17), but the collection or library is not produced either combinatorially or randomly. Instead, the glycopeptides in the collection or library are individually synthesized using multicolumn automated peptide synthesizer by sequentially coupling individual amino acids including pre-fucosylated serine, and subsequently combined to form the collection or library. Rao does not disclose a combinatorially-generated library of randomly glycosylated structures, and it would be humanly impossible to individually synthesize all glycopeptides that would be contained in a combinatorially-generated library as presently claimed. Rao cannot possibly be alleged to disclose libraries that would have the size and diversity of the libraries claimed by applicants. Moreover, the variations in Rao are restricted to amino acid variations - each construct in Rao bears only a single carbohydrate, and randomly glycosylated structures as presently claimed are not disclosed. Nor would the limited library that is disclosed in Rao have suggested, under Section 103(a), a library as presently claimed. The small size of

Rao's library, coupled with the fact that Rao is limited to variations in the amino acids in the peptide, means that Rao would not have suggested applicants' large combinatorially-generated library of randomly glycosylated structures.

Claims 32 and 34-38 are rejected under Section 102(b) or Section 103(a) based on Vetter (WO 95/18971). Vetter describes solid-phase methods of attaching carbohydrates (N-linked), through a linker arm, to solid supports that have no structural definition, and serve solely as an anchor, having no part in the activity of the molecule. The solid support is typically a polymer. A single compound is produced in each reaction vessel, using a solid support. On page 25, Vetter does describe a combinatorial aspect in which he varies the sequence of the peptide except for the O-allyl protected aspartic acid, which remains constant as the sole glycosyl acceptor. But the library carries a single carbohydrate structure with no provision for further iterative synthesis leading to more complex structures, as in the randomly glycosylated libraries according to applicants' invention. Similarly to Rao, Vetter's solid-phase synthesis does not lead to large numbers of randomly-glycosylated structures, such as are contained in the combinatorially-generated libraries according to the present invention. No anticipation or *prima facie* case of obviousness exists, for the same types of reasons as are detailed above for Rao.

Claims 32 and 34-38 are rejected under Section 102(a) based on Schleyer *et al.* (*Agnew. Chem. Int.*) Applicants submit herewith a copy of the PCT International Search Report which indicates that Schleyer *et al.* was designated as a "P" reference, i.e. the document was published prior to the international filing date but later than the priority date claimed. Also, applicants' provisional application fully supports applicants' claims. Thus, Schleyer is insufficient to show that the invention was known or used by others in this country prior to applicants' invention.

Claims 32-37 are rejected under Section 102(b) based on Frische *et al.* (abstract *J. Pept. Sci.*) Frische *et al.* describes the synthesis of a series of peptides and glycopeptides based on the sequence of mouse hemoglobin, through solid phase techniques. Preglycosylated serine and threonine are used. Each glycopeptide is separately synthesized, as in Rao and Vetter, and then combined to form a so-called "library." The arguments

presented above with respect to Rao and Vetter apply with equal force here, and no anticipation or *prima facie* case of obviousness exists.

None of the cited references anticipate or render obvious applicants' claims to a combinatorially-generated glycopeptide library, which has tremendous diversity. Diversity is important for discovery of biologically active components. Applicants' glycopeptide libraries provide the type of diversity, by using combinatorial methods in which several and various carbohydrates are randomly placed on a given sequence of amino acids. This approach greatly enhances the probability of discovering biologically active molecules. To illustrate the point, consider the core proteins of mucins, which are rich in both glycosylation sites and carbohydrate diversity. The 17 amino acid tandem repeat of human intestinal mucin MUC3 contains 12 unique sites (serines and threonines) for glycosylation. If 3 different carbohydrate structures were to chemically link to a single tandem repeat of MUC3, it is theoretically possible to create a library of over 16 million different glycopeptides with different magnitudes of glycosylation. The single most powerful benefit of having all random combinations is the ability to locate a glycopeptide with the right glycosylation pattern that is characteristic of a cancer-associated mucin. This is not achieved or suggested by Rao, Vetter or Frische.

In view of the foregoing amendments and remarks, it is believed that all claims are in condition for allowance. Reconsideration of all rejections and a notice of allowance are respectfully requested. Should there be any questions regarding this application, the examiner is invited to contact the undersigned attorney at the telephone number listed below.

Respectfully submitted,

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Date

Bernhard D. Saxe
Reg. No. 28,665

FOLEY & LARDNER
Suite 500, 3000 K Street, N.W.
Washington, D.C. 20007-5109
Tel: (202) 672-5300